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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,350	11/08/2002	Anne Clark	NBI-108US	8642

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EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,350	CLARK ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24,27,32-36,41,43,44,46,47 and 53-73* is/are pending in the application.

4a) Of the above claim(s) *32-36,41,43,44,46,47 and 54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24,27,53 and 55-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

JC

DETAILED ACTION

Claim Objections

Claim 27 is objected to because of the following informalities: Compound (x) is incorrectly named. It should be 3,3-dimethyl-1-propanesulfonic acid. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59-66 and 69-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to methods of preparing cells to be used for the treatment a number of diseases such as diabetes, Alzheimer's or spongiform, encephalopathy, wherein the treatment can include transplanting the prepared cells. The specification discloses that transgenic islet cells were cultured with various compounds and that islet amyloid formation was inhibited to a degree.

The plurality of diseases claimed for the potential use of the disclosed cells not only have no known cures, but most do not even have any satisfactory treatment to alleviate symptoms of the various diseases. Currently, insulin therapy is the only treatment for diabetes. Kisilevsky (1996) gives a general view of the strategies that researchers might use to formulate anti-amyloid drugs for the potential treatment of diseases associated with amyloidosis. Currently, some compounds are known to inhibit amyloid deposition in cells or small test animals, but no accepted treatments have yet found their way into mainstream medicine such that even the skilled artisan could use cells comprising an amyloidosis

inhibitor for treatment of currently incurable diseases. Kong et al. (US 20050038117) note that transplantation of islets in many instances is unsuccessful due to death of the transplanted cells (section 140). In a recent review, Hoppener et al. confirm the likelihood of a connection between type 2 diabetes and amyloid deposition. However, they disclose that a strategy to inhibit amyloidosis in islet cells is promising, such a therapy does not exist at the present time (p. 418, left col., 2nd paragraph). Neither the instant disclosure, nor the current sate of the art, have reliably demonstrated how to prevent the death of transplanted cells.

Therefore, claims 59-66 and 69-73 are not enabled by the instant disclosure such that the skilled artisan could prepared cells suitable for the treatment of the claimed diseases or transplantation.

Claims 22-24, 27, 53, 55-58, 67 and 68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for preparing islet cells suitable for treating a subject that can benefit therefrom, comprising contacting islet cells *in vitro* with an inhibitor of islet amyloid polypeptide deposit formation, wherein said inhibitor is selected from the group consisting of compounds (i)-(x), as shown in claim 27, wherein said deposits having been form by said cells prior to said contact, does not reasonably provide enablement for a method for preparing any type of cell for treating any subject having amyloid deposits by contacting said cell with any possible compound, to inhibit or prevent any type of amyloid deposit. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to a method of preparing cells for treating a subject having amyloid deposits comprising contacting said cells *in vitro* with any compound that can inhibit amyloid deposit formation. The specification discloses that transgenic islet cells were cultured with certain compounds and that islet amyloid formation was inhibited to a degree. The specification does not disclose how the skilled artisan would select compounds other than those claimed in instant claim 27 to inhibit amyloid

deposit of any type for treating a subject. Kisilevsky (1996) reviews that properties of various types of amyloids. Although there are similarities, there are also significant differences in protein types. It is unclear if the skilled artisan would reasonably expect that an inhibitor of one type of amyloid would other amyloids. Further, the physiology of cells that bear amyloid deposit are quite varied. The instant specification does not address the uncertainties of how cellular physiology could impact the ability of an inhibitor of islet amyloid to successfully inhibit amyloid deposition in a neuron.

Although a method for the preparation of islet cells according to the directions of the instant specification might benefit a subject, the instant specification does not demonstrate that the cells are suitable for treating a subject having amyloid deposits. A subject having amyloid deposits includes one suffering from diabetes, Alzheimer's or spongiform encephalopathy, for example. None of these diseases have a cure and only diabetes has a proven treatment (insulin therapy). Neither the instant specification not the prior art have demonstrated how the preparation of cells according to the instant claims could be used for treatment with any degree of reliability.

The plurality of diseases claimed for the potential use of the disclosed cells not only have no known cures, but most do not even have any satisfactory treatment to alleviate symptoms of the various diseases. Currently, insulin therapy is the only treatment for diabetes. Kisilevsky (1996) gives a general view of the strategies that researchers might use to formulate anti-amyloid drugs for the potential treatment of diseases associated with amyoidosis. In a recent review, Hoppener et al. confirm the likelihood of a connection between type 2 diabetes and amyloid deposition. However, they disclose that a strategy to inhibit amyloidosis in islet cells is promising, such a therapy does not exist at the present time (p. 418, left col., 2nd paragraph). Currently, some compounds are known to inhibit amyloid deposition in cells or small test animals, but no accepted treatments have yet found their way into mainstream medicine such that even the skilled artisan could use cells comprising an amyloidosis.

The instant specification shows ten specific compounds that inhibited islet amyloid formation in transgenic cells. However, the instant specification does not provide any guidance as to the basis for the

selection of the compounds. That is, what structural similarities could the skilled artisan recognize that would enable him or her to select the next inhibitor with a reasonable expectation of success?

Instant claim 22 is drawn to inhibiting amyloid formation in a cell. This claim includes two embodiments: (1) preventing deposition in a cell in which there is no amyloid protein present or (2) inhibiting deposition in a cell in which amyloid protein was already present. Preventing-type language carries with it implication of totality of absence and possible occurrence of amyloid deposition. There is neither explicit nor implicit teaching in Applicants specification or in the prior art where the totality and future occurrence of the deposition of amyloid has been successfully prevented or eliminated. One of skill in the art would be subjected to undue and laborious experimentation to determine how to make a cell composition for the prevention of amyloid deposition.

There is no reliable method that predicts which types of compounds will inhibit or prevent amyoidosis in any cell for the purpose of treating a subject. The specification does not teach how one of ordinary skill in the art could decide *a priori* which compounds will inhibitor prevent amyoidosis in any type of cell for said purpose. The limited disclosure cannot be extrapolated by the skilled artisan to predict how to inhibit or prevent amyloidosis in any cell type intended for treatment of a subject. It would require one of skill in the art undue experimentation to determine what compounds will inhibit or prevent amyoidosis in cells other than islets to treat subjects according to the directions of the instant disclosure. Thus, claims 22-24, 27, 53, 55-58, 67 and 68 are not commensurate in scope with the enabling disclosure.

Claim Rejections - 35 USC § 102

Claims 22, 24, 27, 53, 55 and 56 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cik et al. (1993).

Applicant asserts that the instantly amended claims overcome the rejection.

The amendment to claim 22 does not distinguish the prior art from the claimed invention because the cells describe by Cik et al. are still suitable for transplantation into a subject. The newly added phrase

"such that amyloid deposit formation is inhibited therein" is descriptive because the cells taught by Cik et al. contain 2-amino-5-phosphopentanoic acid (AP5), which would inherently inhibit the deposition of amyloid in the cultured cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Hanley
Patent Examiner
AU 1651

JEAN C. WITZ
PRIMARY EXAMINER